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 TI Inhibition of mast cell tryptase by inhaled APC 366 attenuates allergen-induced late-phase airway obstruction in **asthma**.  
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 AB BACKGROUND: APC 366, a selective inhibitor of mast cell tryptase, has been shown to inhibit antigen-induced early asthmatic response (EAR), late asthmatic response (LAR), and bronchial hyperresponsiveness (BHR) in a sheep model of allergic **asthma**. OBJECTIVE: The purpose of this study was to investigate the effects of APC 366 on antigen-induced EAR, LAR, and BHR in mild atopic asthmatics not on any anti-inflammatory therapy. METHODS: Sixteen mild atopic asthmatics, each with a demonstrable antigen-induced EAR, LAR, and BHR to histamine, were recruited into this randomized, double-blinded, crossover study. APC 366 (5 mg)/placebo was administered by aerosol inhalation 3 times per day on treatment days 1 through 4. Allergen challenge was carried out on day 4. Histamine challenge was performed the following morning, 1 hour after final dosing. RESULTS: Subjects were shown to have a significantly smaller overall mean area under the curve for the LAR ( $P = .012$ ) and mean maximum fall in FEV(1) for the LAR ( $P = .007$ ) after pretreatment with APC 366 in comparison with placebo. No significant effects on BHR were demonstrable. Although the EAR was reduced by 18% after treatment with APC 366 in comparison with placebo, this was not statistically significant. CONCLUSION: Short-term repeated administration of APC 366 significantly reduced the magnitude of antigen-induced LAR in atopic asthmatics, which supports the role of mast cell tryptase in the pathophysiology of the LAR.  
 CT Check Tags: Female; Male  
 Administration, Inhalation  
 Adult  
 \*Allergens: IM, immunology  
 \*Asthma: DT, drug therapy  
 Asthma: EN, enzymology  
 Asthma: PP, physiopathology  
 Bronchial Hyperreactivity: DT, drug therapy  
 Bronchial Hyperreactivity: EN, enzymology  
 Bronchial Hyperreactivity: PP, physiopathology  
 Cross-Over Studies  
 \*Dipeptides: AD, administration & dosage  
 Dipeptides: TU, therapeutic use  
 Double-Blind Method  
 Humans  
 \*Mast Cells: EN, enzymology  
 Mast Cells: IM, immunology  
 Research Support, Non-U.S. Gov't  
 \*Serine Endopeptidases: ME, metabolism  
 \*Serine Proteinase Inhibitors: AD, administration & dosage

Serine Proteinase Inhibitors: TU, therapeutic use  
CN 0 (Allergens); 0 (Dipeptides); 0 (N-(1-hydroxy-2-naphthoyl)arginyl-  
prolinamide); 0 (Serine Proteinase Inhibitors); EC 3.4.21 (Serine  
Endopeptidases); EC 3.4.21.59 (tryptase)